Editorial: Is the UK NHS a good place to do clinical trials?

In 2004, the Government, acknowledging that more needed to be done to increase the capability of the NHS to conduct R&D, committed to a budget of £100m by 2008. One of the early steps in this process has been the establishment of the UK Clinical Research Collaboration (UKCRC) to coordinate changes that will make more and better clinical research possible. Can it succeed and will the benefits extend to industrially sponsored trials?

The background is as follows. For years, the NHS and its managers have been nailed to the wall by successive governments wanting improvements in productivity, cost savings and services for patients. Although these aims are laudable, they completely eliminated in many Trusts the desire to become involved in research activities, which were perceived as being irrelevant. Furthermore, compensation to Trusts and to young doctors did not recognise research efforts and these were then duly disregarded.

More recently, the introduction of the Clinical Trials Directive has added a further layer of difficulty for clinical research, especially as it applies to academic and Phase I clinical trials. In particular, the requirement for the use of good manufacturing practice (GMP) quality materials with qualified person (QP) release and the need to file a clinical trial application with the Medicines and Healthcare products Regulatory Agency (MHRA) prior even to Phase I studies poses major difficulties for academic clinical researchers and, to some extent, to small companies wishing to conduct trials in the UK. Certainly, the UK's competitive position in respect of Phase I trials has not been helped by the requirements of the Clinical Trial Directive.

What can be done? The UKCRC has conducted a wide-ranging consultation exercise within the NHS and has come to a series of conclusions. In a nutshell, these are that it is, indeed, desirable that clinical research should occur within the NHS simply because (a) patients may benefit in the long term and (b) more cost-effective treatment programmes may be identified. In particular, the NHS is seen as being especially suitable for large-scale clinical trials, outcomes research, service research and preventive medicine. However, the barrier to this is the aforementioned lack of financial and career incentives inherent in the current structures.

In response to this, UKCRC is focusing on a round of consultative exercises designed, in particular, to set up and fund clinical research networks, akin to the National Cancer Research Network (NCRN) that already exists. In the first instance, these networks will relate to paediatric medicine, diabetes mellitus, stroke and Alzheimer's disease. It is not clear whether or when, in the fullness of time, other networks would emerge but it would be hoped that this would be the case. It is assumed that, as with the national cancer networks, the government funding will go towards enrolling interested clinical units, assessments of their core competencies, training and provision of key infrastructure such as staff, equipment and, possibly, facilities.

This is excellent but is it enough? From an industrial point of view, a key question must be whether industrially sponsored trials will benefit. Although industrial organisations (the ABPI and BIA) are involved in the consultative exercise, the impression gained so far is that these networks will verge towards academic rather than industrially led research. This is certainly the case with the NCRN, where an academic champion is essential before a trial with a new molecular entity can be envisaged.

In addition, although the network concept is a good and valid one, it addresses only a part of the problem. Many other aspects remain untackled. For example, whenever a new industry-sponsored clinical trial is placed in an NHS Trust, a bureaucratic process ensues that involves the definition of a budget and contractual obligations by the Trust R&D office, Local Research Ethics Committee (LREC) approval and indemnification of the Trust by the Sponsor. Here, the unfortunate impression is that the processing and management of these tasks is no one's first priority in a majority of Trusts. Because of this, clinical trial set-up in the NHS is uniformly slow and frustrating for Sponsors. Until resources are ploughed into this area and somebody's bonus or promotion depends on the efficient management of clinical trial bureaucracy, it is hard to see how this will change.

Once a trial is running, competition for beds is still an issue if in-patient stays are part of the protocol. The lack of beds dedicated to clinical trials could be overcome if the resources were available. Recruitment often lags behind what was promised and envisaged. While this is often blamed on too many trials chasing too few patients, an alternative explanation is a failure of trials to be adequately publicised and for referrals to be negligible even when a trial is well known. A cultural change might be deemed necessary. Sophisticated diagnostic modalities such as computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) scanning that might be taken for granted elsewhere are often lacking, rationed or booked far in advance, thus causing delays. Again, resources are at the heart of the issue.

Finally, the imposition of GMP requirements at the moment is causing major headaches. Delays by an overstretched MHRA in accrediting manufacturing units are causing problems in clinical trial initiation. While, it is hoped, this is just a teething problem, it has to be remembered that every pharmacy in the land that prepares an intravenous infusion for a clinical trial now requires QP release. All need accreditation. If we are to have more regulation, it has to be administered efficiently.

For products involving genetically modified viruses, the situation is even more dire, with health and safety issues to be resolved on a Trust by Trust basis, often at great expense of time and energy. Suffice it to say that only a few hospitals in the UK are set up to deal with even the most straightforward of these products, which bodes ill for the conduct of Phase III trials with these agents in this country. A recently published article by Bamford *et al.*[1] graphically illustrates the lengths to which one Teaching Hospital Trust has had to go to enable a gene therapy clinical trial programme to go ahead. It is hard to imagine that, if this is the norm, major clinical trials of these advanced products can ever be conducted in this country since the vast majority of Trusts will simply not bother. How on earth this can be addressed has not even surfaced on any action plan, although Alan Milburn in January 2002 announced that Britain must be at the leading edge of genetics. As usual, the emphasis is on basic research but he and others must realise that basic research will go nowhere if the means to develop it clinically are not there.

What are the alternatives? The obvious candidates are Europe and North America. There are also the tiger economies emerging in South East Asia, many of which long to be part of the global clinical development network and will move mountains to achieve this aim. The NHS, being a mountain in itself, may find this competition difficult to withstand.

Is the NHS a good place for pharmaceutical companies to undertake clinical research? The answer has to be 'yes and no': 'yes' because many of us are used to it and 'no' because we can see how far it is falling behind and how much needs to be done. The government and the various bodies charged with improving conditions and competitiveness in the NHS need to do rather more than just discussing issues. Now is a time for decisive and rapid action on all levels, financial, organisational, regulatory and

educational to ensure that the NHS does indeed achieve the premier clinical research position to which it aspires.

Jan Steiner,
Director,
Oxford Therapeutics Consulting,
Magdalen Centre,
The Oxford Science Park,
Oxford OX4 4GA, UK

Reference

1. Bamford, K. B., Wood, S. and Shaw, R. J. (2005), 'Standards for gene therapy clinical trials based on pro-active risk assessment in a London NHS Teaching Hospital Trust', *Quart. J. Med.*, January, pp. 1–12.